REMARKS

Applicants have received and reviewed an Office Action dated February 24, 2004. Applicants request entry of the amendment and response and reconsideration of the rejection of the claims.

Claims 1-6 and 8-10 are currently under consideration in the present application. Applicants thank the Examiner for rejoinder of group 44 to the elected invention of group 45.

Claims 7 and 11-66 were withdrawn by the Examiner and are herein cancelled without prejudice or disclaimer. Claims 2 and 6 are also canceled. Applicants reserve the right to preserve the subject matter of the canceled claims in one or more continuation application.

Claims 3-6 and 10 are amended to correct dependency and to comply with the Examiner's restriction requirement. Applicants submit the amendments are supported throughout the specification and do not raise any issues of new matter. With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any objection and/or rejection made by the Examiner. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Applicants have added new claims 67-80. Applicants submit that the new claims are supported throughout the specification and the originally presented claims. Applicants submit the new claims are supported throughout the specification, including at page 3, lines 31-32, page 14, lines 3-8 and page 44, lines 17-25. Claim 67 is original claim 2 rewritten in independent form. Applicants submit the newly presented claims do not raise any issues of new matter.

Petition for Extension of Time

It is noted that a two-month petition for extension of time is necessary to provide for the timeliness of the response. A request for such an extension is made extending the time for response from May 24, 2004 to July 24, 2004, which falls on a Saturday extending the time for response to Monday, July 26, 2004.

Priority

The earliest priority date for the present application is January 13, 2000, not April 14, 2000 as stated by the Examiner. Applicants claim priority to US Application No: 09/759,056, which was filed **January 11, 2001**, not January 21, 2001. Therefore, US Application No:

09/759,056 successfully claims priority to US Provisional Application Nos: 60/175,849 filed **January 13, 2000**, 60/197,089 filed April 14, 2000, and 60/228,914 filed August 29, 2000.

Declaration

Applicants will provide new declarations, in light of the requirements of M.P.E.P. Sections 602.01 and 602.02, as soon as they become available.

Specification

The specification has been amended to include proper trademark demarcation and correct the noted spelling errors, thereby alleviating the Examiner's objections.

Claims

35 U.S.C. §112, ¶1, Written Description

Claims 1-6 and 8-10 are rejected under 35 U.S.C. §112, ¶1, as containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner contends that the definition in the specification of members of the Wnt signaling pathway include members known today and hereinafter identified. The Examiner asserts that this language then renders the genus of tumor cells having aberrant Wnt signaling as an undefined group that cannot be distinguished from others. The Examiner also contends that apart from the tumor cells described in the specification, one of skill in the art could not recognize other tumor cells having altered Wnt signaling. Applicants respectfully traverse.

The written description requirement is satisfied when Applicants' specification conveys with reasonable clarity to those skilled in the art, that as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. Id. at 1406 (emphasis added).

Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Applicants claims are directed to method of selective enhancement of the expression of a protein in a tumor cell characterized by aberrant Wnt signaling. Extensive guidance is provided throughout the specification, including at pages 13 and 14, as noted by the Examiner, for one of skill in the art to identify tumor cells characterized by aberrant Wnt signaling. The specification also indicates that members of this genus include any tumor cells that harbor genetic defects and/or show altered expression patterns of any member of the Wnt signaling pathway. (pg. 13, lines 18-20) Members of the Wnt signaling pathway include, without limitation: Wnt-1, other members of the Wnt gene family, Frizzled receptors, the cytoplasmic protein Dishevelled (Dsh), glycogen synthase kinase-3β (GSK-3β), the transcription factor TCF/LEF1, and transcriptionally activated downstream components of the pathway, such as: the nodal-related 3 gene, Xnr3, the homeobox genes, engrailed, goosecoid, twin (Xtwn), and siamois, c-myc, and the WISP genes, e.g. WISP-1 and WISP-2. One of skill in the art knows that genetic defects and/or altered expression patterns of a member of a signaling pathway will cause aberrant signaling by the pathway. In the Wnt signaling pathway, aberrant signaling is linked to altered normal cellular homeostasis, contributing to aberrant growth and survival of neoplastically transformed cells (i.e. tumor cells or cancer).

The members and relationships of proteins/molecules in the Wnt signaling pathway are described at pages 13-14 and pages 1-2, thereby providing further guidance to one of skill in the art to recognize tumor cells characterized by aberrant Wnt signaling. Additionally, multiple examples of tumor cells or tissues that have been found to have altered expression of members of the Wnt signaling pathway have been described. The present knowledge in the art regarding the Wnt signaling pathway and the ability to identify aberrant Wnt signaling, in combination with the multiple species of tumor cells characterized by aberrant Wnt signaling that are described in

the specification, provide written description for the genus of tumor cells characterized by aberrant Wnt signaling.

35 U.S.C. §112, ¶2, Indefiniteness

Claim 4 is rejected under 35 U.S.C. §112, ¶2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner asserts that claim 4 is indefinite because recitation of the term "corresponding" in the phrase "wherein said protein is over expressed in tumor cells relative to corresponding normal cells" cannot be ascertained, leading to ambiguity. Applicants respectfully traverse.

The test for definiteness under 35 U.S.C. 112, ¶2, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Examples of claim language which have been held to be indefinite set forth in MPEP § 2173.05(d) are fact specific and should not be applied as per se rules. MPEP § 2173.02, 8th Ed., Rev. 1, Feb. 2003.

The term "corresponding" as used in claim 4 in the phrase "corresponding normal cells" is not indefinite. The phrase "corresponding normal cells" is used throughout the specification. Analysis of expression levels of any gene or protein in a tumor cell is made in comparison to a normal (non-tumor) cell of the same or similar type to show any increase or decrease compared to basal expression levels for that gene or protein. Multiple examples are provided demonstrating to one of skill in the art that tumor cells with aberrant Wnt signaling are compared to corresponding normal cells, meaning the same or similar cells or tissue that are not tumor cells. For example, "human Stra6 RNA (corresponding to DNA148380-2827) shows strong over-expression in human colon tumor tissues, when compared with corresponding normal human colon tissues." Page 65, lines 20-21. Additional examples may be found at page 26, lines 19-32; page 14, lines 12-17, page 22, lines 34-36, and Figure 13 and its description on page 6 and 64.

Applicants, therefore, respectfully request withdrawal of this rejection on this basis.

35 U.S.C. §102(a)

Claims 1-6 and 8-10 are rejected under 35 U.S.C. §102(a) as being anticipated by Chu et al. (*J. Nutr.* 129: 1846-1854, 1999) (hereinafter Chu), as evidenced by Pennica et al. (*Proc. Natl. Acad. Sci. USA* 95: 14717-14722, 1998) and Szeto et al., (*Cancer Res.* 61: 4197-4205, 2001) (hereinafter Szeto).

Claims 1-6 and 8-10 are drawn to method for selectively enhancing the expression of a protein in a tumor cell characterized by aberrant Wnt signaling comprising treating said cell with a retinoid. The Examiner based the rejection on the assertion that Chu teaches the treatment of human breast and colon cancer cells with retinoic acid to alter the expression of the cell's genes. The Examiner admits that Chu does not teach the cancer cells treated with retinoic acid are characterized by aberrant Wnt signaling. However, the Examiner cites Pennica to indicate that a human colon cancer cell of Chu is characterized by aberrant Wnt signaling. Additionally, the Examiner admits that Chu does not explicitly teach the selective enhancement of Stra6 expression in cancer cells treated with retinoic acid, nor does Chu expressly teach the synergistic expression of Stra6 by a combination of Wnt 1 and retinoic acid. The Examiner contends that these deficiencies are purportedly overcome by the teachings of Szeto solely by suggesting that Stra6 was previously known to be up-regulated by retinoic acid. Applicants respectfully traverse.

As an initial matter, Applicants submit that Szeto reference is not properly considered prior art. The publication date of the Szeto et al. reference is May 15, 2001. Applicants claim priority to U.S. Application Serial No. 09/759,056 which was filed January 11, 2001, which claims priority to U.S. Application Serial No. 60/175,849 filed January 13, 2000. Both of these applications were filed before the publication of the Szeto et al. reference. Thus, Applicants request withdrawal of the rejection based on the Szeto et al. reference.

Under 35 U.S.C. §102, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Applicants submit the Chu et al. reference does not anticipate the claimed invention, because each element of the claims is not found in the disclosure of Chu et al.

Applicants submit that the Chu et al. reference does not teach, inter alia, that cancer cells are characterized by aberrant Wnt-1 signaling. The Examiner has admitted that the Chu et al.

reference fails to teach the cancer cells treated with retinoic acid are characterized by altered Wnt signaling. Applicants further submit that the Chu et al. reference does not teach that expression of protein is characterized by synergistic enhancement of expression of a protein by a combination of Wnt and the retinoid. Applicants submit that, in the least for these reasons, Chu et al. does not anticipate Applicants' claimed invention.

The Examiner cites Pennica for teaching that the human colon cancer of Chu et al. is characterized by aberrant Wnt signaling. Applicants note that the Pennica et al. reference does not teach selective enhancement of expression of a protein in a tumor cell characterized by aberrant Wnt signaling comprising treating said tumor cells with an effective amount of a retinoid. Pennica et al. teaches cloning of genes induced in Wnt-1 transformed cells. Moreover, the only cell line in common between the Chu et al. and Pennica et al. papers is the HT29 cell line. This cell line was identified by Chu et al. as a cell line in which the gpx1 and gpx2 gene was not increased in response to retinoic acid, and the cell line is further characterized as RA resistant with respect to expression of these genes. (See Table 2 and pages 1849, col. 2 to page 1851, col. 1). Thus, the Pennica et al. reference does not anticipate the claimed invention.

Thus, based on the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(a).

Summary

In view of the above amendments and remarks, Applicants respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903
Telephone: 612.371.5267

Date: July 26, 2004

Katherine M. Kowalchyk
Reg. No. 36,848

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